

PCT

NOTICE INFORMING THE APPLICANT OF THE
COMMUNICATION OF THE INTERNATIONAL
APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

From the INTERNATIONAL BUREAU

To:

KIDDLE, Simon, J.
Mewburn Ellis
York House
23 Kingsway
London WC2B 6HP
ROYAUME-UNIRECEIVED
16 MAR 2001

Date of mailing (day/month/year) 08 March 2001 (08.03.01)		IMPORTANT NOTICE	
Applicant's or agent's file reference SJK/BP5875265			
International application No. PCT/GB00/03277	International filing date (day/month/year) 24 August 2000 (24.08.00)	Priority date (day/month/year) 02 September 1999 (02.09.99)	
Applicant PROTEOME SCIENCES PLC et al			

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:

AU,KP,KR,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

AE,AG,AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,BZ,CA,CH,CN,CR,CU,CZ,DE,DK,DM,DZ,EA,EE,EP,ES,
FI,GB,GD,GE,GH,GM,HR,HU,ID,IL,IN,IS,JP,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MA,MD,MG,MK,
MN,MW,MX,MZ,NO,NZ,OA,PL,PT,RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,TZ,UA,UG,UZ,VN,YU,

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 08 March 2001 (08.03.01) under No. WO 01/16603

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer J. Zahra
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

INTERNET COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

Date of mailing (day/month/year) 06 June 2001 (06.06.01)	
International application No. PCT/GB00/03277	Applicant's or agent's file reference SJK/BP5875265
International filing date (day/month/year) 24 August 2000 (24.08.00)	Priority date (day/month/year) 02 September 1999 (02.09.99)
Applicant CAWTHORNE, Michael et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
 02 April 2001 (02.04.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Olivia TEFY Telephone No.: (41-22) 338.83.38
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INTERNATIONAL SEARCH REPORT

Int'l Application No

P B 00/03277

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/68 C07K14/47 A61P3/04 A61K38/17 G01N33/50

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EDVARDSSON U ET AL: "A PROTEOMA ANALYSIS OF LIVERS FROM OBESE(OB/OB) MICE TREATED WITH THE PEROXISOME PROLIFERATOR WY14,643" ELECTROPHORESIS, WEINHEIM, DE, vol. 20, no. 4-5, April 1999 (1999-04), pages 935-942, XP000964564 ISSN: 0173-0835 the whole document	1-30, 32-34, 42-45, 47, 48
X	US 5 861 485 A (TARTAGLIA LOUIS ANTHONY) 19 January 1999 (1999-01-19) column 38, line 25 -column 39, line 27 --- -/--	1-27, 29, 30, 32-34, 42-45, 47, 48

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

19 January 2001

Date of mailing of the international search report

07/03/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Hart-Davis, J

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication where appropriate of the relevant passages	Relevant to claim No
X	JITRAPAKDEE SARAWUT ET AL: "Regulation of rat pyruvate carboxylase gene expression by alternative promoters during development. in genetically obese rats and in insulin-secreting cells: Multiple transcripts with 5'-end heterogeneity modulate translation." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 51, 18 December 1998 (1998-12-18), pages 34422-34428, XP002157931 ISSN: 0021-9258	1,31
A	the whole document	36,39
X	STANTON L W ET AL: "EXPRESSION OF CA III IN RODENT MODELS OF OBESITY" MOLECULAR ENDOCRINOLOGY, vol. 5, no. 6, 1991, pages 860-866, XP000980348 ISSN: 0888-8809	1,31
A	the whole document	36,39
X	LYNCH CHRISTOPHER J ET AL: "Carbonic anhydrase III in obese Zucker rats." AMERICAN JOURNAL OF PHYSIOLOGY, vol. 264, no. 4 PART 1, 1993, pages E621-630, XP000980239 ISSN: 0002-9513	1,31
A	the whole document	36,39
A	WO 99 41612 A (JOHNSON PHILIP J ; OXFORD GLYCOSCIENCES UK LTD (GB); MOYSES CHRISTO) 19 August 1999 (1999-08-19) claims 1-34	1,42,47
P,A	LEE RIVERA IRENE ET AL: "Cloning and characterization of a 35-kDa mouse mitochondrial outer membrane protein MOM35 with high homology to Tom40." JOURNAL OF BIOENERGETICS AND BIOMEMBRANES, vol. 32, no. 1, February 2000 (2000-02), pages 111-121, XP000980184 ISSN: 0145-479X the whole document	1,31,36, 39

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 35,37,38,40,41,46,49-52

Present claims 35,37,38,40,41 and 46, relate to methods of treatment of conditions characterized by body weight or eating dysfunction, wherein the agents to be used in treatment are defined solely by their being able to be identified by a screening method such as that of claim 1.

No technical features of the agents envisaged for use in medical treatment compositions, i.e. indications as to chemical structure, are present in the above-mentioned claims, the technical features formulated so as to permit the execution of a meaningful search.

No means are present in the above-mentioned claims by which compounds known in the prior art, although identifiable by the method of claim 1, could be distinguished from novel substances. No definition of the subject matter for which protection is sought is therefore derivable from these claims (Article 6 PCT) or the description (Article 5 PCT). Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define a compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Present claims 49-52 relate to proteins claimed per se as products, with no restriction as to their use, medical or otherwise. It is explicit in the description (pages 97-103) that the proteins identified as being differentially expressed in subjects having conditions characterized by body weight or eating dysfunction are known as products per se in the prior art. Data describing these products per se (available at the SWISS PROT sequence database cited by the applicant at <http://www.expasy.ch/>) was used by the applicant to confirm the identity of proteins studied, and it is thus clear that the products must have been known beforehand in order for identification by comparison to be possible. No definition of the subject matter for which protection is sought is therefore derivable from claims 49-52 (Article 6 PCT) and they have not been searched.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

P B 00/03277

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5861485 A	19-01-1999	US 5741666 A	21-04-1998
		AU 3497295 A	14-03-1996
		WO 9605861 A	29-02-1996
		US 6057109 A	02-05-2000
		US 5702902 A	30-12-1997
		US 5853975 A	29-12-1998
		US 6121017 A	19-09-2000
<hr/>			
WO 9941612 A	19-08-1999	AU 2534999 A	30-08-1999
		EP 1055126 A	29-11-2000
<hr/>			

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference SJK/BP5875265	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 00/03277	International filing date (day month year) 24/08/2000	Earliest Priority Date (day month year) 02/09/1999
Applicant PROTEOME SCIENCES PLC		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

ANALYSIS AND TREATMENT OF BODY WEIGHT AND EATING DISORDERS

5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.



as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.

29



None of the figures.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 35.37.38.40.41.46.49-52

Present claims 35.37.38.40.41 and 46. relate to methods of treatment of conditions characterized by body weight or eating dysfunction, wherein the agents to be used in treatment are defined solely by their being able to be identified by a screening method such as that of claim 1.

No technical features of the agents envisaged for use in medical treatment compositions, i.e. indications as to chemical structure, are present in the above-mentioned claims, the technical features formulated so as to permit the execution of a meaningful search.

No means are present in the above-mentioned claims by which compounds known in the prior art, although identifiable by the method of claim 1, could be distinguished from novel substances. No definition of the subject matter for which protection is sought is therefore derivable from these claims (Article 6 PCT) or the description (Article 5 PCT). Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define a compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Present claims 49-52 relate to proteins claimed per se as products, with no restriction as to their use, medical or otherwise. It is explicit in the description (pages 97-103) that the proteins identified as being differentially expressed in subjects having conditions characterized by body weight or eating dysfunction are known as products per se in the prior art. Data describing these products per se (available at the SWISS PROT sequence database cited by the applicant at <http://www.expasy.ch/>) was used by the applicant to confirm the identity of proteins studied, and it is thus clear that the products must have been known beforehand in order for identification by comparison to be possible. No definition of the subject matter for which protection is sought is therefore derivable from claims 49-52 (Article 6 PCT) and they have not been searched.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

Proteins that are differentially expressed in body weight and eating disorders, such as obesity, are identified. Agents to treat such conditions may be identified by a screening method comprising:

- a) establishing a paradigm in which at least one protein is differentially expressed in relevant tissue from, or representative of, subjects having different levels of body weight or eating dysfunction;
- b) obtaining a sample of relevant tissue taken from, or representative of, a subject having body weight or eating disorders, who or which has been treated with the agent being screened;
- c) determining the presence, absence or degree of expression of the differentially expressed protein(s); and
- d) selecting or rejecting the agent according to the extent to which it changes the expression of the differentially expressed protein(s).

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
8 March 2001 (08.03.2001)

PCT

(10) International Publication Number
WO 01/16603 A3

(51) International Patent Classification⁷: **G01N 33/68**,
C07K 14/47, A61P 3/04, A61K 38/17, G01N 33/50

(74) Agents: **KIDDLE, Simon, J. et al.**; Mewburn Ellis, York
House, 23 Kingsway, London WC2B 6HP (GB).

(21) International Application Number: PCT/GB00/03277

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ,
DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY,
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(22) International Filing Date: 24 August 2000 (24.08.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
9920745.8 2 September 1999 (02.09.1999) GB
0002975.1 9 February 2000 (09.02.2000) GB

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG,
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for all designated States except US*): **PRO-
TEOME SCIENCES PLC** [GB/GB]; Coveham House,
Downside Bridge Road, Cobham, Surrey KT11 3EP (GB).

Published:

— with international search report

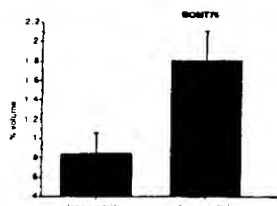
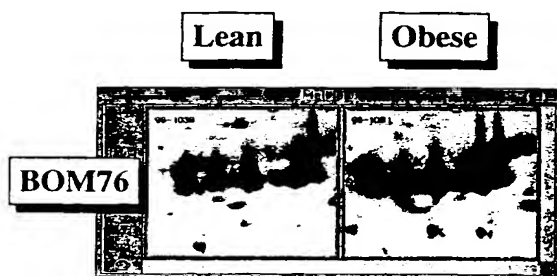
(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **CAWTHORNE,
Michael** [GB/GB]; The University of Buckingham,
Yeomanry House, Hunter Street, Buckingham MK18
1EG (GB). **SANCHEZ, Jean-Charles** [CH/CH];
Frank-Thomas 42, CH-1208 Geneva (CH).

(88) Date of publication of the international search report:
20 September 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: ANALYSIS AND TREATMENT OF BODY WEIGHT AND EATING DISORDERS



(57) Abstract: Methods and compositions relating to body weight and eating disorders, such as obesity, are disclosed. Specifically, proteins that are differentially expressed in these conditions are identified. In one aspect, the invention provides a method of screening an agent to determine its usefulness in treating a condition associated with regulation of appetite and body weight, the method comprising: (a) establishing a paradigm in which at least one protein is differentially expressed in relevant tissue from, or representative of, subjects having differential levels of body weight or eating dysfunction; (b) obtaining a sample of relevant tissue taken from, or representative of, a subject having body weight or eating disorders, who or which has been treated with the agent being screened; (c) determining the presence, absence or degree or expression of the differentially expressed protein or proteins in the tissue from, or representative of, the treated subjects; and (d) selecting or rejecting the agent according to the extent to which it changes the expression of the differentially expressed protein or proteins in the treated subject having body weight or eating disorders.

REC'D 21 JAN 2002

INTERNATIONAL PRELIMINARY EXAMINATION REPORT PCT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference SJK/BP5875265		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB00/03277	International filing date (day/month/year) 24/08/2000	Priority date (day/month/year) 02/09/1999
International Patent Classification (IPC) or national classification and IPC G01N33/68		
Applicant PROTEOME SCIENCES PLC et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 8 sheets, including this cover sheet.
- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 02/04/2001	Date of completion of this report 16.01.2002
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Vanmontfort, D Telephone No. +49 89 2399 8457 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/03277

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-103 as originally filed

Claims, No.:

1-52 as originally filed

Drawings, sheets:

1/58-58/58 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims. Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/03277

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 35, 37, 38, 40, 41, 46, 49-52.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 35, 37, 38, 40, 41, 46, 49-52.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Yes: Claims 1-34, 36, 39, 42-45, 47, 48

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/03277

	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-34
	No:	Claims	36, 39, 42-45, 47, 48
Industrial applicability (IA)	Yes:	Claims	1-34, 36, 39, 42-45, 47, 48
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

1. Section III

The applicant's attention is drawn to the fact that no International Preliminary Examination will be carried out in respect of subject-matter which is not covered by the search report (see Rule 66.1(e) PCT). Therefore, no opinion will be formulated with respect to novelty, inventive step and industrial applicability of the subject-matter of claims 35, 37, 38, 40, 41, 46 and 49-52.

2. Section V

Reference is made to the following documents:

- D1 US 5 861 485 A (TARTAGLIA LOUIS ANTHONY) 19 January 1999
- D2 STANTON et al., MOLECULAR ENDOCRINOLOGY, vol. 5, no. 6, 1991, pages 860-866, XP000980348
- D3 WO 99 41612 A (JOHNSON PHILIP J ; OXFORD GLYCOSCIENCES UK LTD (GB); MOYSES CHRISTO) 19 August 1999
- D4 LEE RIVERA IRENE et al., JOURNAL OF BIOENERGETICS AND BIOMEMBRANES, vol. 32, no. 1, February 2000, pages 111-121, XP000980184

D4 is indicated in the search report as P-document. Since the present application is entitled to the claimed priority date (02.09.1999), D4 is not relevant with respect to novelty and inventive step (Articles 33(2) and (3) PCT).

- 2.1. The subject-matter of claims 1-34 is novel and inventive (Articles 33(2) and 33(3) PCT).

D1 (column 38 line 25-column 39 line 26), which is considered to represent the most relevant state of the art, discloses a method to identify differentially expressed genes and gene products such as proteins in body weight disorder states. The document further discloses the screening of test compounds to determine their usefulness in treating a condition characterised by abnormal body weight or eating dysfunction by comparing gene expression patterns (fingerprint profiles) from animals treated with said test compound and control animals. The different paradigms which can be used for the identification of differentially expressed proteins involved in body weight or eating disorders are disclosed in

columns 10-11. The subject-matter of claim 1 differs from D1 in that gene expression patterns instead of the protein expression patterns are compared. The problem to be solved can therefore be considered as the provision of an alternative method of screening an agent to determine its usefulness in treating a condition characterised by abnormal body weight or eating dysfunction. There is no indication in any of the available prior art documents to use differentially expressed proteins as the paradigm in the screening method. Since one gene can give rise to several proteins by alternate splicing and post translation modification the detection of differentially expressed proteins clearly has advantages. Therefore, it would not be obvious for a skilled person to introduce the above-mentioned feature in the closest prior art. Hence, the subject-matter of claim 1 is considered to involve an inventive step. The same applies to dependent claims 2-34.

- 2.2 The subject-matter of claims 36 and 39 is not inventive (Article 33(3) PCT). D2, which is considered to represent the most relevant state of the art, discloses that carbonic anhydrase-III (WOM50 or WOM52 in the present application, see table on page 100) has been identified as a differentially expressed protein being underexpressed in the adipose tissue of obese mice compared to that in their lean controls. The subject-matter of claims 36 and 39 differs in that said identified compound is used in a method of medical treatment. There is however an indication in D1 (column 38 line 25-column 45 line 16) to use said identified compounds to ameliorate body weight disorder symptoms. Therefore, it would be obvious for a person skilled in the art to introduce this feature in the closest prior art. Therefore, the subject-matter of claims 36 and 39 is considered not to involve an inventive step.
- 2.3 The subject-matter of claims 42-45, 47 and 48 is not inventive (Article 33(3) PCT). D2 (abstract, Figure 1 and Materials & Methods), which is considered to represent the most relevant state of the art, discloses a comparative analysis of adipose tissue of lean and obese rodents by 2-dimensional gel analysis and protein identification. Carbonic anhydrase-III (WOM50 or WOM52 in the present application, see table on page 100) has been identified as a differentially expressed protein being underexpressed in adipose tissue of obese rodents relative to adipose tissue of lean rodents.

The subject-matter of independent claims 42 and 47 differs from D2 in that the described method is used for determining the nature or degree of body weight and/or eating disorder (claim 42) or to predict the most appropriate and effective therapy and to monitor the success of that treatment (claim 47). The problem to be solved by the present invention may therefore be regarded as the provision of an alternative application for the method of claims 42 and 47. There is an indication in D3 (claims) that the technique of 2-dimensional electrophoresis can be used for diagnosis and prognosis of a disorder or for monitoring the effect of therapy by analyzing the presence/intensity or the absence of differentially expressed proteins in samples of persons with and without said disorder. Therefore, it would be obvious for a person skilled in the art to introduce the technical feature in the closest prior art to solve the problem posed. Therefore, the subject-matter of independent claims 42 and 47 is considered not to involve an inventive step. The same applies to dependent claims 43-45 and 48.

3. Section VII

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1 and D2 is not mentioned in the description, nor are these documents identified therein.

4. Section VIII

- 4.1 Claims 36 and 39 are directed to methods of medical treatment by using one of the differentially expressed proteins identified by the method of claim 1. Said method is only theoretically discussed and is in no way illustrated in the experimental part of the description. Therefore, the application does not meet the requirements of Article 6 PCT because none of these claims enjoy any substantial support in terms of concrete examples in the application as filed. There is no evidence whatsoever in the application as filed that the suggested methods actually yield the desired result.
- 4.2 The designations for differentially expressed proteins used in claims 31, 36 and 39 do not have any meaning for a person skilled in the art, thereby resulting in lack of clarity of said claims (Article 6 PCT). These substances are detected by 2D

electrophoresis by comparing subjects having different levels of body weight or eating dysfunction. Said substances are only characterized on the basis of their molecular weight and isoelectric point. Molecular weight and isoelectric point are no unique characteristics for a protein. The applicant has therefore not sufficiently characterized said proteins. A protein can only be characterized (1) by its amino acid sequence, (2) exceptionally in terms of a process of production or (3) by unique and specific characteristics that are unequivocally connected with said protein.